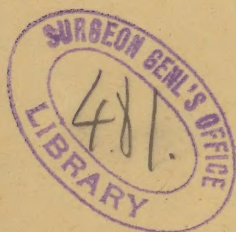
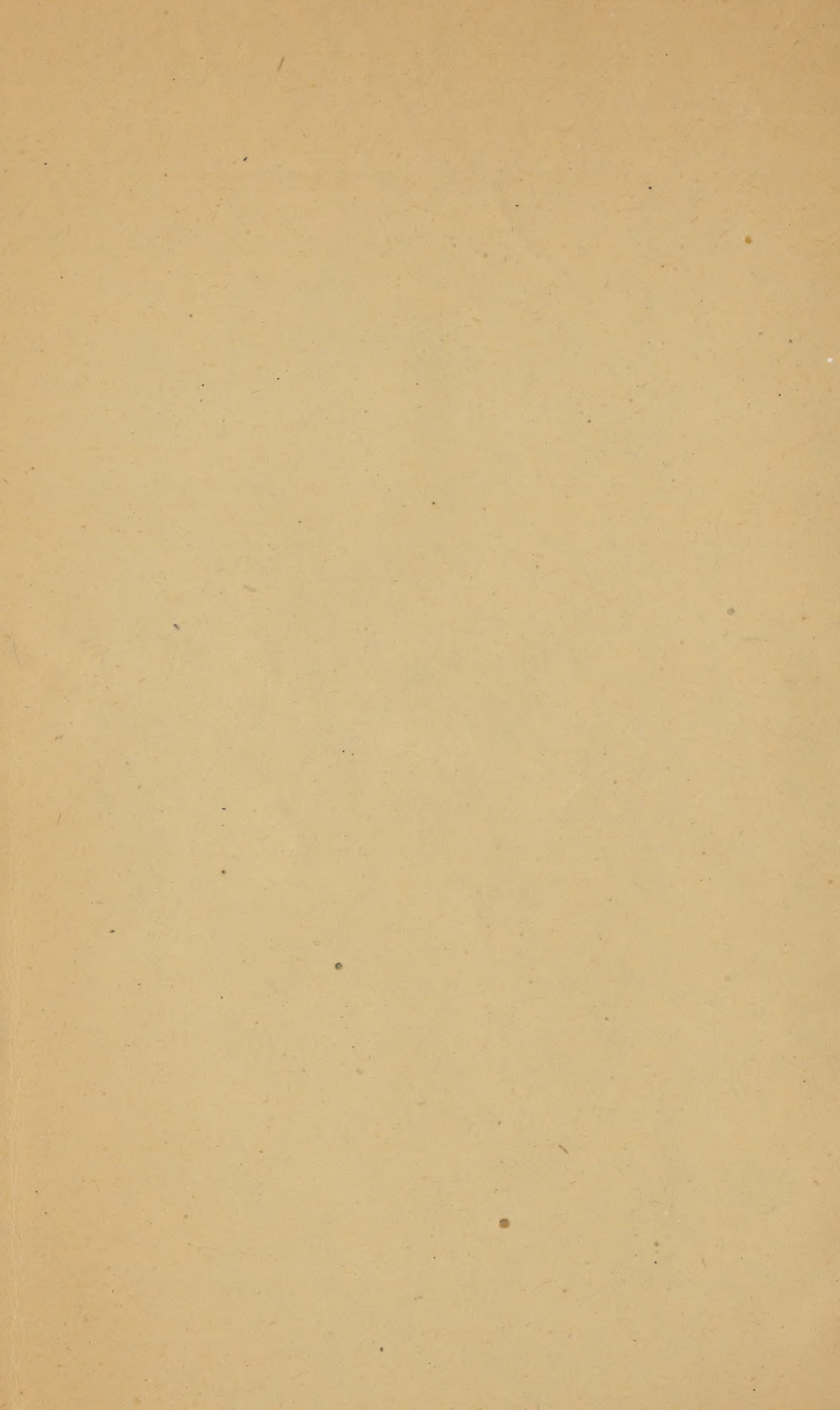


JACKSON (E)

Alarming and dangerous
doses of the mydriatics.





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ALARMING AND DANGEROUS DOSES OF THE MYDRIATICS.

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THE dose of any drug may vary widely, with varying circumstances; but it is always restricted to less than is likely to prove fatal. As no understanding of the power we possess, in the influence of active remedies over vital processes, is complete without an understanding of its limitations; it is worth while to direct our attention to the real limits which danger of fatal poisoning imposes on the use of the mydriatics.

Atropia, I believe, is commonly given in doses of one-half to one milligramme ($\frac{1}{120}$ to $\frac{1}{60}$ of a grain). This is the amount usually given, hypodermically or by the stomach, to check sweating, or to correct or supplement the action of morphia. This amount, or what is deemed an equivalent of some other preparation of belladonna, is mentioned in the various formulas for laxative and anti-neuralgic pills, and mixtures; and much the same dose is administered, when solutions of the ordinary strength are applied to the conjunctival sac. The other mydriatic alkaloids are not in general use; but I think the common impression is, that the dose of daturia, duboisia, or hyoseyamia is about the same as of atropia.

I do not question the sufficiency of such doses to meet, in most cases, what are commonly understood to be the indications for the use of these drugs. But in the minds of many practitioners, well informed on most subjects, the dose of one milligramme comes to hold much the same relation to atropia, as one centigramme holds to morphia, or one gramme to chloral. It is not regarded merely as a sufficient dose, but rather as the maximum, or near the maximum dose, that it is safe to give to any person whose special susceptibility to the action of the drug has not yet been tested; and I wish by this paper to remind you that such an impression is erroneous, and not supported by the literature of mydriatic poisoning.

The impression that much more than one milligramme of one of

the mydriatic alkaloids would be an improper or dangerous dose, probably rests on the liability of the dose mentioned to cause, in susceptible patients, the disorder of vision, dryness of the throat, alteration of the pulse-rate and inco-ordination of thought and motion, which are the symptoms of slight mydriatic poisoning. To the uninformed these symptoms of mydriatic intoxication are very alarming; and that many practitioners of medicine are in this respect uninformed, would appear from the large number of cases of very moderate belladonna or stramonium intoxication, that have been looked upon by their medical attendants as of sufficient gravity to justify extended record; and in which, the symptoms having abated under a certain line of treatment, such treatment is credited with the saving of life. That moderate mydriatic intoxication is not really indicative of danger, becomes evident when the true danger line is shown; and this may be approximately established by a review of: First, cases ending in recovery after the manifestation of very grave symptoms, or in which the known definite amount of the drug used approached or exceeded the minimum fatal dose. Second, all which terminated fatally among the two hundred and fifty cases of mydriatic poisoning that I have found reported, or quoted with sufficient definiteness to make them of value in this connection.

CASES ENDING IN RECOVERY.

CASE 1.—A child, aged three years, swallowed three “homœopathic pellets of belladonna,” and became comatose, with scarcely perceptible pulse and gasping respiration; but recovered. (*Lancet*, 1883, i. p. 485.)

CASE 2.—A man applied a belladonna plaster to his back where pustulation had been already produced by a similar plaster. Marked symptoms appeared in two hours, but the plaster remained on six hours longer. There was inability to use the lower extremities, convulsive catchings, and unconsciousness. He recovered. (William Jenner, *Med. Times and Gazette*, 1856, Nov. 22d.)

CASE 3.—A girl, aged six years, took three-sixteenths of a grain of atropia in solution. There occurred delirium, staggering, drowsiness, sleep; recovery. (Stevenson, *Guy's Hospital Reports*, 1872, p. 226.)

CASE 4.—A man took one-half grain of atropia in solution; inability to stand, flushed face, alarming vertigo, pulse 140, respiration “correspondingly increased.” (Chas. A. Sewal, *Phila. Med. Times*, vol. xii. p. 492.)

CASE 5.—A boy, aged four years, took about half a grain of atropia in solution. There was delirium and disordered movements. (*Lancet*, 1864, i. p. 8.)

CASE 6.—A girl, aged two years, took about a half-grain of sulphate of atropia in watery solution, and recovered. (T. Fitzmaurice, *Lancet*, 1881, ii. p. 414.)

CASE 7.—A woman, aged twenty-one years, took about two-thirds of a grain of atropia in watery solution. There was loss of voice, unconsciousness, twitching of the facial muscles, pulse 130 and weak, restlessness and delirium continuing until the third day, but recovery. (James Andrews, *Month. Journ. Med. Sci.* (Edinburgh), 1852, p. 34.)

CASE 8.—A male infant, aged nineteen months. "The amount of atropia taken was not less than three-fourths of a grain," in solution. "Entire surface bright scarlet, violent delirium, constant and violent spasmodic action of the limbs, intense restlessness." Recovered. (D. W. Prentiss, *Phila. Med. Times*, vol. x. p. 167.)

CASE 9.—A man, aged thirty-four years, took three-fourths of a grain each of the sulphates of morphia and atropia. Recovered. (Dr. Seargent, *Louisville Med. News*, Aug. 27, 1881.)

CASE 10.—A woman, aged twenty-six years, swallowed five centigrammes of atropia sulphate. Furious delirium and aphonia. Recovered. (M. C. Paul, *Gaz. Heb. de Méd. et de Chir.*, 1875, p. 125.)

CASE 11.—A youth, aged nineteen years, took nine-tenths of a grain of atropia in watery solution. Unconsciousness, respiration 40 to 50, pulse 140 to 150 per minute. He recovered. This case was reported by Prof. Purjez. It is quoted in the *British Medical Journal*, 1881, ii. p. 26. What I take to be the same case is referred to in the *Phila. Medical Times*, vol. x. p. 415; but it is there stated that the amount taken was two and one-half grains. I have been unable to examine the original report of the case.

CASE 12.—A physician took one grain of atropia in solution. (J. B. Cox, *Phila. Med. Times*, vol. xiii. p. 377.)

CASE 13.—A child, aged three and one-half years, swallowed one grain of atropia in solution. (Quoted in the *Amer. Journ. Med. Sciences*, Jan. 1869, p. 275.)

CASE 14.—In the Leeds General Infirmary, a man aged seventy, after cataract extraction, developed iritis, for which "six drops of a solution of atropine containing ten grains to the ounce, were ordered to be placed in the eye every third hour." Unpleasant symptoms developed, including paralysis of the lower extremities. Mr. Porritt, who reports the case, remarks: "The solution of atro-

pine was placed in the eye eight times, the quantity used being equivalent to one grain of the alkaloid. This strong solution has been used on many occasions without any untoward effects." (*Lancet*, 1880, i. p. 682.)

CASE 15.—A man took one grain of atropia sulphate in solution, but recovered. (H. Leach, *Med. Times and Gazette*, 1865, ii. p. 34.)

CASE 16.—An advocate swallowed one decigramme of atropia sulphate in solution. He remained unconscious and undiscovered until the next day, and recovered without treatment. (M. Gubler, *Gaz. Heb. de Méd. et de Chir.*, 1875, p. 125.)

CASE 17.—A woman, aged 43, and her daughter, aged thirteen, drank a solution containing about three grains of atropia sulphate. At three hours they were seen with staggering gait and greatly excited; at four hours they were becoming comatose; at four and one-half hours the child vomited, and soon after began to improve. The mother continued violent and partly unconscious until next morning; but they "both left the hospital recovered," twenty-four hours after taking the drug. (*Lancet*, 1878, i. p. 165.)

CASE 18.—A woman, aged thirty, swallowed with suicidal intent about twelve centigrammes of atropia in solution. Delirium, extreme agitation, unconsciousness, pulse 150 per minute and depressed; but she recovered. (Roux, *Gaz. des Hôpitaux*, May 31, 1860.)

CASE 19.—A woman, aged forty-two years, took two and a quarter ounces of belladonna liniment. Her symptoms were very severe, but she recovered. (Dr. Grattan, *Brit. Med. Journ.*, 1881, i. p. 594.)

CASE 20.—Four children, aged from six to nine years, ate seeds of the *datura stramonium*. Confusion of intellect ensued, with entire loss of power to direct the motions of the limbs, and stupor. They recovered. (H. Y. Evans, *Amer. Journ. Med. Sciences*, July, 1866, p. 278.)

CASE 21.—In twelve cases of poisoning by stramonium reported by H. T. O. Morsly, there was delirium, unconsciousness, intermittent action of the heart, apparent syncope, and approaching death; yet all recovered. (Quoted in *Journ. of Amer. Med. Assoc.*, vol i. p. 22.)

CASE 22.—A man, recovering from cataract extraction, took one teaspoonful of a solution of duboisia sulphate one grain to the ounce of water. (E. L. Holmes, *Chicago Med. Journ. and Exam.*, Nov. 1880.)

CASE 23.—A woman, aged forty-six years, took one-half grain of hyosecyamia in solution. "Apparently comatose," pulse 120, and

temperature 103° F. Recovered. (J. G. S. Coghill, *Lancet*, 1880, ii. p. 152.)

In the cases above cited, as in most of those to follow, which terminated fatally, no mention has been made of the many different lines of treatment pursued. Any attempt to attach to each of these its proper value, would have extended this paper far beyond the limits of my time and your patience. Let me dismiss the matter with this one remark: Excepting the prompt emptying of the stomach, I am not convinced that any line of treatment has averted a fatal result in mydriatic poisoning.

FATAL CASES.

CASE 24.—A man, aged thirty-three years, had a blistered surface, on the neck dressed with an ointment of atropia sulphate, fifteen parts to seven hundred parts of lard. In a few minutes he “sprang from his seat in a state of indescribable anguish, he ran about the room crying out that he was suffocated.” “Dysphagia and dyspnoea increased . . . convulsions resembling those of chorea set in, breathing became very frequent, soon became interrupted;” the pulse rose to 150 per minute, and death occurred within two hours after the application of the drug. This man was suffering at the time with laryngeal disease. This case is reported by H. Ploss, of Leipsic (quoted in *Brit. Med. Journ.*, 1865, i. p. 68, and elsewhere).

CASE 25.—A man ate of a tart made of belladonna berries. There ensued delirium, unconsciousness, convulsions, coma, and death within twenty-four hours. A boy ate of the same tart, and also died. (*Lancet*, 1846, ii. p. 251.)

CASE 26.—A boy, aged four years, ate belladonna berries. There were delirium, inability to stand, convulsive attacks, temperature 110° F., and death after seventeen hours. (McNab, *Brit. Med. Journ.*, Sept. 23, 1882.)

CASE 27.—A boy, aged five years, ate belladonna berries, and died in convulsions in fifteen hours. (*Taylor's Med. Jur. and Toxicology*.)

CASE 28.—A woman, aged twenty-seven years, used a decoction made from eighty grains of the root as a clyster. Death in five hours. (*Taylor's Med. Jur. and Tox.*)

CASE 29.—A woman, aged sixty-six, took a teaspoonful of belladonna liniment, became deeply comatose, and died in sixteen hours. (*Lancet*, 1870, ii. p. 83.)

CASE 30.—A boy, aged sixteen years, swallowed one drachm of extract of belladonna in a half-teacupful of warm water. Uncon-

sciousness, violent agitation of the limbs, coma, and death within three hours. (R. H. Taylor, *Brit. Med. Journ.*, 1869, ii. p. 555.)

CASE 31.—Mr. Harris was poisoned by atropia taken in milk, amount unknown. He died in twelve hours. (*Lancet*, 1872, i. p. 241.)

CASE 32.—A man, aged forty-five, swallowed one drachm of liquor atropiæ sulphatis, B. P. Being treated by emetics, the stomach-pump, a drachm of tincture of digitalis, brandy, black coffee, castor oil by enema, and mustard to the feet and over the heart; he grew better of the symptoms of poisoning, but later pneumonia set in, and he died on the fourth day. The autopsy showed besides extensive recent hepatization, chronic organic disease of both lungs and heart. (A. S. Greenway, *Brit. Med. Journ.*, 1878, October 5th.)

CASE 33.—A young man took two grains of atropia at bedtime, and was found dead next morning. (*Taylor's Med. Jur. and Tox.*)

CASE 34.—A woman, aged forty-three years, swallowed three grains of atropia. Violent delirium, trismus, and later muscular relaxation; sudden appearance of symptoms of suffocation, and death about fifteen hours after taking the drug. (S. W. Gross, *Am. Journ. of Med. Sci.*, October, 1869, p. 401.)

CASE 35.—The case of a soldier who died from eating the shoots of the *Datura stramonium* was reported by Barton. (*Beck's Medical Jurisprudence.*)

CASE 36.—A woman drank a decoction of bruised stramonium seeds, and died in seven hours. (*Taylor's Med. Jur. and Tox.*)

CASE 37.—A male convict ate a large quantity of stramonium seeds. He was found insensible, with stertorous breathing, and pulse 120 per minute, and died an hour later. (Robert Allan, *Lancet*, 1847, ii. p. 298.)

CASE 38.—A delicate girl, aged two and one-half years, ate over one hundred seeds (weighing sixteen grains) of *Datura stramonium*. Spasm of the glottis, twitching and tetanic spasms, and coma, pulse 200, respirations upward of 100 per minute. Death within twenty-four hours. Reported by her father. (E. W. Duffin, *Lond. Med. Gaz.*, 1834, vol. xv. p. 194.)

~~CASE~~ 39.—Two fatal cases of poisoning by hyoscyamus are referred to by Christison in his work on poisons.

~~CASE~~ 40.—*Datura* poisoning is very common in the East, and Taylor and Tardieu both mention that Dr. Brown, in a work on "The Poisons of Punjab," published in 1863, had collected twenty-one that terminated fatally. It is probable that some of these cases are mentioned above.

A careful examination of the literature of this subject seems to me to justify these conclusions:—

First. *For adults the minimum fatal dose of atropia is certainly not less than the minimum fatal dose of morphia.*

Second. *The minimum fatal dose for children of two years of age and upwards is not less than for adults.*

Third. *There is every probability that the same is true of the other mydriatic alkaloids.*

These conclusions are supported by those cases in which large doses of the mydriatics have been given medicinally. Dr. S. B. Foreman, of Lancaster, used fifteen and twenty grain doses of the extract of belladonna, per rectum, relieving a case of obstinate constipation. (*Practitioner* (Lancaster, Pa.), 1883, p. 10.) Dr. J. M. Fothergill gave one grain of atropia hypodermically in a case of opium poisoning, saving his patient. (*Lancet*, 1878, i. 354.) One and one-sixth grains were given in a case of strychnia poisoning, and the patient recovered. (*Edinburgh Med. Journ.*, September, 1873.) Dr. Henry W. Fuller, of London (*Med. Times and Gazette*, 1859, July 23d), gave very large doses of extract of belladonna and atropia to twelve children suffering from chorea. "The result was in all cases the same, namely, extraordinary tolerance of the remedy. . . . The tolerance of the drug being so great that one girl, aged ten, took seventy grains of the extract of belladonna daily, and a total amount of one thousand and nineteen grains, or rather more than two ounces in twenty-six days; whilst the child, aged fourteen, to whom the atropine was administered, took no less than thirty-seven grains in eighteen days." Abundant crystals of atropia were obtained from the urine and feces of a patient, "who at the time was taking sixty-four grains of the extract of belladonna daily."

Dr. Sydney Ringer, in his *Hand-book of Therapeutics* (sixth edition, p. 530), narrates a very interesting case, where large doses of the mydriatic alkaloids were given to a woman, aged twenty-two years, suffering from acute mania. During three weeks atropia sulphate was given in one-quarter grain dose once, in three-fourths grain dose once, in one grain doses five times; daturia, in one grain doses four times; and hyoscyamia in one grain doses seven times. Under this treatment the patient improved.

I would not plead for any indiscriminate or useless increase of the dose of these drugs; but cases occur in which there is urgent need that they be used freely; and practitioners sometimes fail to meet the plainest indications for treatment, because of this erroneous impression, that any decided increase over the common dose would

be dangerous. Those of us who are engaged in ophthalmic practice, see instances of this in eyes seriously damaged by iritic adhesions, that have formed while a one-fourth or one-half per cent. solution of atropia was being instilled, one drop at a time with intervals of several hours.

Of course, in using the mydriatics freely, there is risk of causing the symptoms of mydriatic intoxication; but this may be largely guarded against by the simultaneous use of ordinary medicinal doses of morphia, or perhaps pilocarpin, or chloral; and if it cannot be thus entirely prevented, the physician can simply and truthfully say that delirium, unnatural voice, and irregular locomotion indicate no more danger when produced by a mydriatic than when produced by alcohol. We every day cause the deepest intoxication with ether, to give relief from evils less serious than the loss or impairment of an eye. Let us use the mydriatics as rationally, remembering that with them *there is an exceptionally wide interval between the alarming and the fatal dose.*



